I. AMENDMENT OF CLAIMS

This listing of claims shall replace all prior version, and listings, of claims in the application.

Listing of Claims

Claim 1. (Currently amended): A solid oral controlled-release dosage form suitable for 24 hour dosing of an active agent in a human patient comprising a pharmaceutically acceptable matrix comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material; said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85; and said dosage form providing a therapeutic effect for at least about 24 hours.

Claim 2. (Original): The dosage form of claim 1, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 3. (Original): The dosage form of claim 1, wherein said matrix is a plurality of multiparticulate matrices.

Claim 4. (Original): The dosage form of claim 3, wherein said multiparticulates are compressed into a tablet.

Claim 5. (Original): The dosage form of claim 3, wherein said multiparticulates are disposed in a pharmaceutically acceptable capsule.

Claim 6. (Original): The dosage form of claim 1 which provides a C_{24}/C_{max} ratio of 0.60 to 0.70.

Claim 7. (Original): The dosage form of claim 1 which provides a dissolution release rate in-vitro of the hydrocodone when measured by the USP Basket method at

100rpm in 700 ml aqueous buffer at a pH of 1.2 at 37° C is at least 10% to about 45% by weight hydrocodone or salt thereof released at 1 hour.

Claim 8. (Original): The dosage form of claim 1, which provides a dissolution release rate in-vitro of the hydrocodone or salt thereof when measured by the USP Basket Method at 100 rpm in 700 ml Simulated Gastric Fluid (SGF) at 37° C for 1 hour and thereafter switching to 900 ml with Phosphate Buffer to a pH of 7.5 at 37 ° \C, of at least 20% by weight hydrocodone or salt thereof released at 4 hrs, from about 20% to about 65% by weight hydrocodone or salt thereof released at 8 hrs, from about 45% to about 85% by weight hydrocodone or salt thereof released at 12 hrs, and at least 80% by weight hydrocodone or salt thereof released at 24 hours.

Claim 9. (Original): The dosage form of claim 1, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 10. (Original): The dosage form of claim 1, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 11. (Original): The dosage form of claim 1, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 12. (Original): The dosage form of claim 1, wherein said administration is first administration.

Claim 13. (Original): The dosage form of claim 1, wherein said administration is steady state administration.

Claim 14. (Original): The dosage form of claim 1, wherein said ratio is provided to a population of patients.

Claim 15. (Currently amended): A solid oral controlled-release dosage form suitable for 24 hour dosing of an active agent in a human patient comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material, said dosage form after oral administration, providing a rate of absorption during the time period from T_{max} to about 24 hours after oral administration of the dosage form which is from about 45% to about 85% of the rate of elimination during the same time period, said dosage form providing a therapeutic effect for at least about 24 hours.

Claim 16. (Currently amended): A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form comprising a pharmaceutically acceptable matrix comprising an analgesically effective amount of an active agent comprising hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material, said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85 and a therapeutic effect for at least about 24 hours.

Claim 17. (Currently amended): A process for the preparation of a solid oral controlled-release dosage form, comprising incorporating an analgesically effective amount of an active agent comprising hydrocodone or a pharmaceutically acceptable salt thereof into a controlled release material, said dosage form after administration to a human patient, providing a C_{24}/C_{max} ratio of 0.55 to about 0.85 and a therapeutic effect for at least about 24 hours.

Claim 18. (Currently amended): A solid oral controlled-release dosage form suitable for 24 hour dosing an active agent in a human patient comprising a plurality of pharmaceutically acceptable beads coated with an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and overcoated with a pH-

independent hydrophobic material comprising an acrylic polymer, said dosage form providing an in-vitro release rate, of hydrocodone or a pharmaceutically acceptable salt thereof, when measured by the USP Basket Method at 100 rpm in 900 ml aqueous buffer at a pH of between 1.6 and 7.2 at 37° C of from 0% to about 35% at 1 hour, from about 10% to about 70% at 4 hours, from about 20% to about 75% at 8 hours, from about 30% to about 80% at 12 hours, from about 40% to about 90% at 18 hours, and greater than about 60% at 24 hours; the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer, is no greater than 10%; said dosage form providing a C24/C_{max} ratio of 0.55 to about 0.85; and a therapeutic effect for at least 24 hours, after oral administration to a human patient.

Claim 19. (Original): The dosage form of claim 18, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 20. (Original): The dosage form of claim 18, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 21. (Original): The dosage form of claim 18, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 22. (Original): The dosage form of claim 18, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 23. (Original): The dosage form of claim 18, wherein said administration is first administration.

Claim 24. (Original): The dosage form of claim 18, wherein said administration is steady state administration.

Claim 25. (Original): The dosage form of claim 18, wherein said ratio is provided to a population of patients.

Claim 26. (Original): A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 18 to a human patient.

Claim 27. (Currently amended): A sustained release oral dosage form comprising:

(a) a bilayer core comprising:

(i) a drug layer comprising an analgesically effective amount of an active agent comprising hydrocodone or a pharmaceutically acceptable salt thereof; and

(ii) a displacement layer comprising an osmopolymer; and

(b) a semipermeable wall comprising a hydrophobic material selected from the group consisting of a cellulosic polymer, an acrylic polymer and a combination thereof surrounding the bilayer core having a passageway disposed therein for the release of said hydrocodone or pharmaceutically acceptable salt thereof; said dosage form providing a C_{24}/C_{max} ratio of 0.55 to about 0.85; and said dosage form providing a therapeutic effect for at least about 24 hours after oral administration to a human patient.

Claim 28. (Original): The dosage form of claim 27, which provides a C_{24}/C_{max} ratio of 0.55 to 0.75.

Claim 29. (Original): The dosage form of claim 27, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 4 to about 14 hours after oral administration of the dosage form.

Claim 30. (Original): The dosage form of claim 27, which provides a time to maximum plasma concentration (T_{max}) of hydrocodone at about 6 to about 12 hours after oral administration of the dosage form.

Claim 31. (Original): The dosage form of claim 27, which provides a C_{max} of hydrocodone which is less than 60% of the C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation.

Claim 32. (Original): The dosage form of claim 27, wherein said administration is first administration.

Claim 33. (Original): The dosage form of claim 27, wherein said administration is steady state administration.

Claim 34. (Original): The dosage form of claim 27, which provides a dissolution release rate in-vitro of the hydrocodone or salt thereof when measured by the USP Basket Method at 100 rpm in 700 ml Simulated Gastric Fluid (SGF) at 37° C for 1 hour and thereafter switching to 900 ml with Phosphate Buffer to a pH of 7.5 at 37° C, of at least 20% by weight hydrocodone or salt thereof released at 4 hrs, from about 20% to about 65% by weight hydrocodone or salt thereof released at 8 hrs, from about 45% to about 85% by weight hydrocodone or salt thereof released at 12 hrs, and at least 80% by weight hydrocodone or salt thereof released at 24 hours.

Claim 35. (Original): The dosage form of claim 27, wherein said ratio is provided to a population of patients.

Claim 36. (Original): A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 27 to a human patient.

Claim 37. (Previously presented): A sustained release oral dosage form comprising:

(a) a bilayer core comprising:

i) a drug layer comprising an active agent comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof; and

(ii) a displacement layer comprising an osmopolymer; and

(b) a semipermeable wall comprising a hydrophobic material selected from the group consisting of a cellulosic polymer, an acrylic polymer and a combination thereof surrounding the bilayer core having a passageway disposed therein for the release of said hydrocodone or pharmaceutically acceptable salt thereof; said dosage form providing an in-vitro release rate, of hydrocodone or a pharmaceutically acceptable salt thereof, when measured by the USP Basket Method at 100 rpm in 900 ml aqueous buffer at a pH of between 1.6 and 7.2 at 37° C of from 0% to about 35% at 1 hour, from about 10% to about 70% at 4 hours, from about 20% to about 75% at 8 hours, from about 30% to about 80% at 12 hours, from about 40% to about 90% at 18 hours, and greater than about 60% at 24 hours; the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopoeia XXII (1990) at 100 rpm in 900 ml aqueous buffer, is no greater than 10%.

Claim 38. (Original): A method of providing effective analgesia in a human patient for at least about 24 hours comprising orally administering a dosage form of claim 37 to a human patient.

Claim 39. (New): The dosage form of claim 1, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 40. (New): The dosage form of claim 39, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 41. (New): The dosage form of claim 15, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 42. (New): The dosage form of claim 41, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 43. (New): The dosage form of claim 16, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 44. (New): The dosage form of claim 43, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 45. (New): The method of claim 17, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 46. (New): The method of claim 45, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 47. (New): The dosage form of claim 18, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 48. (New): The dosage form of claim 47, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 49. (New): The dosage form of claim 27, wherein the active agent is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 50. (New): The dosage form of claim 49, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 51. (New): The method of claim 36, wherein the active agent in the dosage form is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 52. (New): The method of claim 51, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 53. (New): The dosage form of claim 37, wherein the active is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 54. (New): The dosage form of claim 53, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA

receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.

Claim 55. (New): The method of claim 38, wherein the active agent in the dosage form is selected from the group consisting of hydrocodone, a non-opioid drug, their mixtures and pharmaceutically acceptable salts thereof.

Claim 56. (New): The method of claim 55, wherein the non-opioid drug is selected from the group consisting of a non-steroidal anti-inflammatory agent, an NMDA receptor antagonist, acetaminophen, aspirin, a neuro-active steroids and a non-opioid analgesic, their mixtures and pharmaceutically acceptable salts thereof.